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学位論文の題名	Zerumbone inhibits angiogenesis by blocking NF- κ B activity in pancreatic cancer (ゼルンボンは NF- κ B 活性を介して膵癌血管新生を抑制する) Pancreas. in press
論文審査担当者	主査： 岡本 尚 副査： 城 卓志, 竹山 廣光

Abstract

Objectives

Since angiogenesis is essential for tumor growth and metastasis, the development of anti-angiogenic agents is an urgent issue in cancer treatment. Zerumbone, a component of subtropical ginger, has been shown to exhibit anticancer activities in various cancer cells; however, little is known about its biological mechanisms against angiogenesis in pancreatic cancer. Here, we evaluated the effects of zerumbone on pancreatic cancer angiogenesis.

Methods

The cytotoxicity of zerumbone in pancreatic cancer was measured using premix WST-1 cell proliferation assays. The influence of zerumbone on the angiogenic factors vascular endothelial growth factor (VEGF) and interleukin-8 (IL-8) was measured using reverse transcription-polymerase chain reaction (RT-PCR) and enzyme-linked immunosorbent assays (ELISAs). Changes in nuclear factor-kappa B (NF- κ B) activities were measured using NF- κ B transcription factor assays. We also examined the effects of zerumbone on pancreatic cancer-induced angiogenesis using angiogenesis assays.

Results

Zerumbone inhibited mRNA expression and protein secretion of angiogenic factors as well as NF- κ B activity. Tube formation in human umbilical vein endothelial cells was enhanced by coculture with pancreatic cancer cells, and these enhancements were significantly inhibited by zerumbone treatment.

Conclusion

Zerumbone blocked pancreatic cancer-associated angiogenesis through inhibition of NF- κ B and NF- κ B-dependent pro-angiogenic gene products.